

**AMENDMENTS TO THE CLAIMS**

1. (Currently Amended) A method for prenatal diagnosis of foetal cells isolated from maternal blood, comprising the following steps:

- a) filtering a sample of pure or diluted maternal blood on a filter to concentrate on a filter according to size, certain circulating cells, and in particular cells of foetal origin, which has a pore size of between 6 and 15  $\mu$ m, whereby epithelial cells are retained onto said filter;
- b) analyzing the cells retained on the filter to obtain a presumption or identification of their foetal or maternal origin for the presence of at least one immunological or cytological marker, which is characteristic of trophoblastic and/or syncytiotrophoblastic cells, to identify trophoblastic and/or syncytiotrophoblastic cells; and individually collecting at least one cell, which has been identified as being a trophoblastic and/or syncytiotrophoblastic cell, whereby a single cell, which is presumed to be of foetal origin, or a collection of single cells, which are presumed to be of foetal origin, is obtained;
- c) demonstrating the foetal origin of certain enriched cells by genetic analysis of individually isolated cells;
- d) identifying genetic anomalies specifically targeted to individually analyze cellular genomes for which a foetal origin has been demonstrated;
- e) lysing the single cell of step b), or a single cell of the collection obtained at step b), whereby the genome of this single cell is made accessible to amplification primers;
- d) amplifying the genome of the lysed single cell obtained at step c), whereby a pre-amplification product is obtained from a single cell;
- e) using the pre-amplification product obtained at step d), both to demonstrate the foetal origin of the single cell, and to carry out the prenatal diagnosis, wherein:

- i. said pre-amplification product is analyzed for the presence of genetic or polymorphism marker(s), which can, or the alleotyping of which can, be distinguished from the one(s) of a maternal cell genome, by amplification of said marker(s) from said pre-amplification product, whereby said presence demonstrates the foetal origin of said single cell, and
  - ii. if said foetal origin is demonstrated, identifying at least one genetic or chromosomal anomaly of the foetus, or a genotype thereof, by genetic analysis of said pre-amplification product.

2. - 3. (Cancelled).

4. (Currently Amended) ~~A-The method according to of claim 13, characterized in that wherein the cells retained on the filter are collected individually by microdissection.~~

5. (Currently Amended) ~~A-The method according to of claim 4, characterized in that wherein said microdissection consists of laser cutting the portion of the filtration membrane filter on which a cell is retained or detaching the cell using a laser then recovering the single collected cell in a suitable tube.~~

6. – 8 .(Cancelled).

9. (Currently Amended). ~~A-The method according to of claim 1-7 or claim 8, characterized in that wherein said identification of a at least one genetic or chromosomal anomaly of the foetus, or of a particular genotype thereof, is carried out by identifying one or more a genetic target(s) in said preamplification product on a preparation of DNA derived from the genome of the single collected cell.~~

10. (Currently Amended) A The method of claim 1 according to any one of claims to 9, characterized in that prior to demonstrating the foetal or maternal origin of a single collected cell and/or identifying a genetic or chromosomal anomaly of the foetus or of a particular genotype thereof, said collected cell is lysed and its entire genome is preamplified and wherein prior to step e), the preamplification product of step d) is purified to obtain a preparation of preamplified DNA derived from the genome of asaid single collected cell.

11. (Currently Amended) A The method according to of claim 9-10, characterized in that the foetal or maternal origin of a collected cell is demonstrated, then wherein said at least one genetic or chromosomal anomaly of the foetus, or of a particular said genotype thereof, is identified by amplification of genetic markers or of polymorphism or of a combination of said markers or one or more sequence(s) carrying the identified genetic target(s), from said preamplification product the preamplified DNA preparation derived from the genome of said cell.

12. (Currently Amended) A The method of according to claim 11, characterized in that wherein said amplification of at least one genetic marker or of polymorphism or of at least one or more sequence(s) carrying a the genetic target(s) is carried out from less than one fifth of said preamplification product the preamplified DNA preparation.

13. (Currently Amended) A The method according to of claim 11 or claim 12, characterized in that wherein the foetal or maternal origin of a collected cell and/or said identification of a at least one genetic or chromosomal anomaly of a foetus, or of a particular said genotype thereof, is demonstrated by sequencing the amplified genetic target(s) carried in the amplified sequence(s) or markers.

14. (Currently Amended) A The method according to of claim 10, characterized in that the foetal or maternal origin of a collected cell is demonstrated, and/or a wherein said at least one genetic or chromosomal anomaly of the foetus, or of a particular said genotype thereof, is identified by hybridization of all or a portion of the preamplified DNA preparation with specific DNA probes or PNA (Peptide Nucleic Acid) Peptide Nucleic Acid (PNA) type probes.

15. (Currently Amended) A The method according to of claim 14, characterized in that wherein the specific DNA probes are fixed on a support forming a DNA micro- or macro-array.

16. (Currently Amended) A The method according to any one of claims 9 to 15 of claim 1 or 4 or 5 or any one of claims 9 to 15, characterized in that said wherein at least one of said polymorphism markers to be identified is a microsatellite marker, a VNTR (Variable Number of Tandem Repeats) Variable Number of Tandem Repeats (VNTR) marker, a SNP (Single Nucleotide Polymorphism) Single Nucleotide Polymorphism (SNP) marker or a STR (Short Tandem Repeat) Short Tandem Repeat (STR) marker.

17. (Currently Amended) A The method according to any one of claims 9 to 16 of claim 1, characterized in that wherein the foetal or maternal origin of a collected cell is demonstrated by identifying a marker or a combination of markers, the presence of which, or the allelotyping of which, is specific to the DNA of paternal cells or an allele assay of said markers distinguished from those detected on the genome of non maternal cells, in particular by seeking the genome of said collected cell, a marker or a combination of markers specific to the DNA of paternal cells.

18. (Currently Amended) A The method according to of claim 10, characterized in that wherein a chromosomal anomaly is identified by a method for comparative genomic hybridization (CGH) of:

- a said preamplified DNA preparation derived from the genome of a said single collected cell, and the foetal origin of which has been demonstrated, and of
- a preamplified DNA preparation of cells ~~or~~ of maternal origin or of non foetal reference cells.

19. (Cancelled).

20. (Currently Amended) A The method according to any one of claims 1 to 19, characterized in that of claim 1, wherein the filtered maternal blood is derived from a blood sample made after the fifth week of pregnancy.

21. Currently Amended) A The method according to any one of claims 1 to 20, characterized in that of claim 1, wherein the genetic analysis of cells retained on the filter is carried out by said filtering of maternal blood is a filtering of 1 to 10 mL of maternal blood.

22. (Currently Amended) A The method according to any one of claims 1 to 21, characterized in that of claim 1, wherein the maternal blood sample is diluted 10 to 100 fold in a filtration solution.

23. (Currently Amended) A The method according to any one of the preceding claims of claim 1, characterized in that wherein the pure or diluted maternal blood sample is filtered using a filter, with a pore size in the range 6 to 15  $\mu\text{m}$ , preferably the pores, of which have with a diameter of about 8  $\mu\text{m}$ .

24. (Currently Amended) A The method according to of claim 23, characterized in that wherein the filter has pores with a diameter of about 8  $\mu\text{m}$  and a pore density in the range  $5 \times 10^4$  to  $5 \times 10^5$  pores/ $\text{m}^2\text{cm}^2$ .

25. (Currently Amended) A The method according to any one of claims claim 1 to 24, characterized in that wherein the filter is a polycarbonate filtration membrane, the pore size of which is graded, and all of the pores of said polycarbonate filtration membrane have a substantially identical diameter.

26. (Currently Amended) A use of a filtration device A process for obtaining foetal cells present in maternal blood, and comprising wherein said process comprises filtering said maternal blood on a filtration device, which comprises, on a frame:

a porous filter that can retain certain circulating cells according to their size, which has a pore size of between 6 and 15  $\mu\text{m}$ , mounted between two clamping devices, respectively upstream and downstream with respect to the filtration direction, and providing a filtration seal;

the upstream block clamping device comprising means for storing and/or pre-treating the samples to be analyzed;

the downstream block clamping device comprising perforations facing the storage means;  
and

means for forced filtration.

27. (Currently Amended) The process of Use according to claim 26 of a ISET type filtration device in which the, which comprises applying pressure on said filter, wherein said applied pressure is in the range 0.05 bars to 0.8 bars, preferably 0.1 bars.

28. (Currently Amended) The process of Use according to claim 26 or claim 27, of a ISET type filtration device for isolating foetal cells from maternal blood and comprising a  
wherein said filter with has a mean pore size in the range 6  $\mu\text{m}$  to 15  $\mu\text{m}$ , preferably about of  
8  $\mu\text{m}$ .

29. (Currently Amended) The process of Use according to claim 28, of a ISET type device in which the wherein said filter has pores with a diameter of about 8  $\mu\text{m}$ , and a pore density in the range of  $5 \times 10^4$  to  $5 \times 10^5$  pores/cm<sup>2</sup>.